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VI

PYRETO-THERAPY BY INTRAVENOUS T.A.B. VACCINE IN THE TREATMENT OF SULPHONAMIDE RESISTANT GONORRHŒA AND NON-GONOCOCCAL URETHRITIS*

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INTRODUCTION

THE purpose of this paper is to attempt an assessment of the value of T.A.B. vaccine injected intravenously in the treatment of cases of gonorrhœa and non-gonococcal urethritis which have failed to respond to various drugs of the sulphonamide group. At the same time schemes of dosage and methods of administration are reviewed in relation to the height and duration of temperature produced.

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While the efficiency of the sulphonamide drugs in most cases of gonorrhœa, non-gonococcal urethritis and their complications is generally accepted, a definite proportion of cases fail to respond to these drugs. These failures present a difficult therapeutic problem.

In recent years, such resistant cases have been treated by high prolonged fever induced by mechanical means (Simpson, 1936) and the results have been satisfactory. Fever produced by protein shock, as in the method under review, is less effective, since it possesses no mechanism for controlling heat loss from the body and is dependent on the uncertain factor of individual reaction. But it has advantages in that it is always easily available and requires no expensive apparatus or highly trained staff.

In the present study 207 male patients were treated with T.A.B. vaccine given intravenously at the Royal Victoria Hospital, Netley, during a period of six months. The group consisted of complicated and uncomplicated cases which had failed to respond to drugs of the sulphonamide group. In some patients complications had occurred during or after sulphonamide therapy. The majority of these patients had also received urethral irrigations. The first 20 patients were treated with a single intravenous dose of vaccine; in two of these cases later in treatment and in all other cases the vaccine was administered by the divided dose method, the history and technique of which will be described.

DIVIDED DOSE METHOD

Nelson (1931) first used the method in the treatment of neurosyphilis. He wrote as follows :—

“ The technique is simple and consists in giving two daily intravenous injections of the vaccine, properly spaced as to time of injection. The first dose is given at any selected time and is of a size calculated to give slight fever; the second is given during the height of the fever produced by the first, usually at the end of the second or third hour. The second dose seems to have the effect of ‘exploding’ the charge supplied by the first and in this way relatively small doses are capable of producing fever apparently as high as desired—105°, 106°, 107° F.”

The comparative temperature charts in his original article referred to three cases, and indicated that total doses of 35 million organisms or more might be expected to give higher or more prolonged fever if given by the

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divided method than if given in a single dose. A further and more detailed account of this method was given by Driver and Shaw in 1933, using typhoid vaccine in the treatment of neurosyphilis. The following points from their technique are worthy of mention :—

The temperature was taken rectally every half hour until it had risen to 104° F., then every quarter of an hour until it had fallen to 104° F. again ; thereafter it was recorded hourly. They advised against the use of antipyretics, which tended greatly to diminish the height and duration of the fever. They concluded that the interval between doses should be not less than two hours, but the interval might be extended from two to six hours, provided that the temperature had not dropped to nearly normal by this time. They used divided doses the total of which ranged from 20 million organisms upwards.

DOSAGE AND TECHNIQUE USED IN THE PRESENT SERIES

In deciding on the suitable dose and method of administration two considerations have to be borne in mind ; first the safety and comfort of the patient, and secondly the height and duration of the pyrexia. Before the commencement of this series it was observed that patients who had been given from 250 million to 625 million organisms (0.10 c.c. to 0.25 c.c. of undiluted Army T.A.B. vaccine) in single doses showed marked constitutional disturbance, with vomiting, severe headache and general malaise. As a result refusal of further injections was not uncommon.

Stock Army T.A.B. vaccine, diluted 1 in 10 with normal saline was used throughout the present series. Each 1 c.cm. of this vaccine contained 250 million organisms. It is most important that the vaccine be fresh and that it be kept in a cool dark place.

1. *Single dose method.* In 20 cases single doses of T.A.B. vaccine were given as follows :—

- (a) In 10 cases, 25 million organisms and, if considered necessary, 50 million after an interval of 2-4 days.
- (b) In 10 cases, 50 million organisms and, if considered necessary, 75 million after an interval of 2-4 days.

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2. *Divided dose method.* In 50 cases divided doses of T.A.B. vaccine were given as follows :—

Two doses of 25 million organisms separated by an interval of four hours. After an interval of 2-4 days a dose of 50 million followed in four hours by one of 25 million, if considered necessary.

The temperature was taken by mouth hourly by day and two-hourly by night. It was not practicable to record rectal temperatures except in 20 cases used for comparison. It must be noted that all temperatures given in this series are oral recordings unless otherwise stated ; allowance must be made therefore in comparing them with rectal temperatures recorded by other workers. The fact that it was necessary to take temperatures hourly instead of at shorter intervals made it less certain that the actual temperature peak was recorded, and it is probable therefore that some of the results understated the actual maximum level of temperature reached.

The first injection was given with the patient lying in bed, or ready to go to bed immediately afterwards. The bed was made up with blankets next to the skin, beginning with two blankets under the patient and two others covering him. The patient was not allowed to take food after 8.30 a.m.

As soon as the temperature had begun to rise, in from half an hour to two hours after the first injection, the patient usually complained of shivering. A hot water bottle was then placed in the bed, and extra blankets were added. As soon as perspiration was free the patient was encouraged to drink 0.6 per cent. saline. It is a curious fact, which the pioneers of high fever therapy learned by experience, that saline of this strength is quite palatable to patients with high temperatures, for the salt taste is not detectable. The patient's pyjamas were exchanged for a warm dry pair when they became saturated with perspiration. No antipyretic drug was given, in order to avoid interference with the temperature reaction.

When divided dosage was used the second dose was given 4 hours after the first injection, by which time the temperature was usually raised to between 99° and 100° F. The temperature peak was generally reached 2-3 hours later but was sometimes delayed, even till the

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following day. In the great majority the temperature had returned to normal by the morning following the injection. These patients were allowed up for half an hour that afternoon, and could return to light duties on the following morning.

Table 1 indicates the average peak and duration of temperature in the 20 cases treated with single dosage and in the 50 treated with divided doses. It compares them with 50 cases which had been treated previously with large single doses of T.A.B. vaccine, varying from 250 to 625 million organisms. It will be seen from this table that the divided dose method produced greater height and longer duration of temperature than the single dose method, whether small or large doses were given. (Charts 1 and 2.)

The divided dose method was used in all other cases (Table 1A), but the number of organisms was varied. Doses smaller and larger than those originally used were tried; these are compared in Table 2.

In some cases a poor temperature response resulted from the first treatment and therefore for the second the dose was split into three injections of 25 million organisms each. The results obtained do not suggest that this is in general a valuable practice (Table 2), but it is possible that division of doses may help in certain cases. In a few cases poor reactions occurred time after time, and further splitting of the dosage failed to increase the temperature level. (Chart 3.)

Injection by the divided dose method can be used daily provided that the temperature returns to normal on the morning following the injections; but in most cases in this series an interval of at least two days preceded further injections. If a patient's initial temperature is raised to over 99° F., a single injection only may give similar results to the ordinary divided dose. (Chart 4.)

Elkins and Krusen (1939) state that in general the rectal temperature exceeds the oral by 1°–2° F., and they consider that under-recording of oral temperatures may result if the patient drinks cold fluids just before the recording is taken, or because he fails to keep his mouth shut while the thermometer is in place. In the present series the rectal temperatures were not recorded in the majority of cases, but an attempt was made to assess the average variations between oral and rectal temperatures

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in a representative group of the patients under investigation. In ten cases simultaneous oral and rectal temperatures were recorded during fever therapy and the average difference was found to be 1.1°F. , although individual variations ranged from 0.6° to 1.4°F. In a further series of ten cases the variations taken at the temperature peak also averaged 1.1°F. , with individual variations ranging from 0.5° to 2.4°F. So it was assumed that 1.0°F. should be added to oral temperature records to give an approximate estimate of the corresponding rectal temperature. (Chart 5.)

TOXIC EFFECTS

The following 93 toxic effects occurred in the 207 patients treated by this method :—

(1) Nausea was fairly common but vomiting was rare, occurring in 4 cases.

(2) Backache and general aching pains occurred in 8 cases, but lasted not more than 24 hours.

(3) Headaches of two kinds were experienced in 72 cases as follows :—

(a) A throbbing headache sometimes occurred during fever.

(b) The day following fever a dull headache occurred which may have been due to chloride loss, for it was not experienced by those patients who had taken a good volume of 0.6% saline.

(4) Fainting occurred in one case only. The patient had disobeyed instructions and had got up to wash on the morning following his injections.

(5) Herpes labialis occurred in 6 cases. It began a few days after the treatment and cleared up well with applications of spirit of camphor.

(6) Hyperpyrexia (with oral temperature over 106°F.) occurred in only 2 cases, and was relieved by tepid sponging. One of these patients showed signs of cerebral irritation but the other appeared quite comfortable.

DETAILS OF CASES TREATED

The cases treated are divided into the following groups :

A. *Gonorrhœa with persistence of signs after sulphonamide treatment* (98 cases).

1. 17 cases with pus cells in the urethral smear and a "dirty" urine on the day following the end of a course

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of sulphapyridine. After pyrexia 3 passed tests without further treatment, 4 passed tests after further urethral irrigations and 10 were clinical failures.

2. (a) 44 cases with pus cells in the urethral smear or a "dirty" urine after about 3-5 weeks' treatment which had included one course of sulphapyridine, one course of sulphanilamide, and urethral irrigations followed by 2-3 days' observation. After pyrexia 15 cases passed tests without further treatment, 7 passed tests after further treatment with urethral irrigations and 22 were clinical failures.

(b) 9 cases with findings similar to those in Group 2 (a) after miscellaneous treatment of from 2-8 weeks' duration including one course of sulphapyridine. After pyrexia 4 passed tests without further treatment, 1 passed tests after further urethral irrigations and 4 were clinical failures.

3. 18 cases with gonococci in the urethral smear after one course of sulphapyridine. After pyrexia 2 passed tests, but one of these relapsed in 14 days with gonococci again in the smear, while the other was given the injection of T.A.B. vaccine on the fourth day of a second course of sulphapyridine. The remaining 16 patients continued to show gonococci in the urethral smears.

A second series of 13 patients received T.A.B. vaccine immediately following a short intensive course of sulphapyridine; this group included 3 of the failures of the above series, and 10 other patients in whom gonococci were present in the urethral smear after one course of sulphapyridine. The procedure was as follows:—

The patient was put to bed and given sulphapyridine in doses of 2 gm. at 5 p.m., 1 a.m., and 9 a.m. The first dose of T.A.B. vaccine was given at 11 a.m. and the second at 3 p.m. In some cases a further divided dose of T.A.B. vaccine was given at 11 a.m. and 3 p.m. the following day, and in one case the treatment was again repeated on the third day. If the temperature was above 99.0° F. at 11 a.m., only a single injection was given on that day. Of these patients, 3 passed tests without any further treatment, 2 passed tests after further urethral irrigations of 7 and 4 days' duration respectively, and 8 were clinical failures. One of these patients developed epididymitis after further treatment with sulphanilamide and urethral irrigations, but passed tests after a further

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injection of T.A.B. vaccine. Details of these cases are given in Table 3.

B. Non-Gonococcal urethritis with persistence of signs after sulphonamide treatment. (65 cases.)

1. 15 cases with pus cells in the urethral smear and a "dirty" urine on the day following the end of a course of sulphapyridine. After pyrexia 4 passed tests after further urethral irrigations and 11 were clinical failures.

2. (a) 36 cases with pus cells in the urethral smear or a "dirty" urine after about 3-5 weeks' treatment which had included one course of sulphapyridine one course of sulphanilamide and urethral irrigations followed by 2-3 days' observation. After pyrexia 15 passed tests without further treatment, 4 passed tests after further treatment with urethral irrigations and in 17 cases the treatment failed.

(b) 14 cases with similar findings to Group 2 (a) after miscellaneous treatment of from 2-8 weeks' duration, including one course of sulphapyridine. After pyrexia 10 passed tests without further treatment, 2 passed tests after further urethral irrigations and in 2 cases treatment failed. Details of these cases are given in Table 4.

C. Complications of Gonorrhœa and Non-gonococcal urethritis. (48 cases.)

The cases are divided into the following groups :—

1. 45 resistant cases of arthritis, fasciitis and myositis of which 27 gave a history of gonorrhœa and 18 a history of non-gonococcal urethritis. All these patients had had treatment which included one course of sulphapyridine.

2. 3 resistant cases of iritis with a history of gonorrhœa which had received local treatment and a course of sulphapyridine.

1. All but five of these resistant complicated cases have been classified into one of three sub-groups according to the time of the onset of the signs or symptoms.

(a) In 10 patients signs or symptoms developed before admission to hospital. These were given T.A.B. vaccine after the failure of a course of sulphapyridine. No cure resulted. 3 patients showed improvement sufficiently for discharge for convalescence and 7 obtained only temporary relief.

(b) In 4 patients the signs or symptoms developed during the course of sulphapyridine. These were

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immediately given T.A.B. vaccine. Three were cured and the fourth was improved sufficiently for discharge for convalescence.

- (c) In 26 patients in whom the signs or symptoms developed after a course of sulphapyridine, T.A.B. vaccine was given and cure resulted in 22. The remaining 4 improved sufficiently for discharge for convalescence.

Of the above 40 patients, 21 showed definite physical signs and 19 complained of symptoms which were not confirmed by physical signs. Of a group of 5 patients additional to the above 40 two were transferred to the care of a psychiatrist and there was no evidence that their symptoms were due to organic disease while in the remaining 3 cases no chemotherapy was given prior to the injection of T.A.B. vaccine.

In these complicated cases the knee was the joint most commonly affected, arthritis of this joint being present in 27 cases. Three had associated keratoderma blenorrhagica, which cleared under treatment. In 2 patients urinary signs persisted after the arthritis had been cured. The series included one case of plantar fasciitis and 4 cases of myositis. Twenty-one patients received additional physiotherapy. These cases are classified in more detail in Table 5.

2. One case of acute recurrent iridocyclitis and 2 cases of recurrent sub-acute iritis were treated with T.A.B. vaccine after the failure of a course of sulphapyridine. These patients showed progressive benefit and in each case the eye was in a quiescent condition on the patient's discharge from hospital. Details of these cases are given in Table 5.

COMMENT

The first aim in the investigation was to discover the smallest dose of the vaccine necessary to produce a suitable temperature reaction. For this purpose the divided dose method appears to be better than the single dose method and the number of organisms required was considerably less with an equivalent lessening of the toxic effects. A suitable dosage in most cases seems to be as follows :—

1st Treatment. 25 million organisms repeated in 4 hours.

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2nd Treatment. 50 million organisms followed by 25 million organisms in 4 hours or 25 million organisms repeated twice at 3 hour intervals if the first treatment failed to produce a good temperature reaction.

3rd Treatment. 50 million organisms repeated in 4 hours or one of 50 million organisms followed by two doses of 25 million organisms at 3 hour intervals with periods of 2 days or more between the treatments.

The only severe reaction which occurred was hyperpyrexia over 106° F. This can be prevented if frequent temperature recordings are taken when the temperature rises above 105° F. Tepid sponging should be instituted, if the temperature rises a further 0.5° F., or if the patient shows signs of marked restlessness.

The second problem was to assess the clinical uses of T.A.B. vaccine in various types of cases.

Gonorrhœa. In cases with persistent gonococci in urethral smears T.A.B. vaccine alone seemed to be of little use. Nevertheless some cures were obtained in the cases treated with T.A.B. vaccine immediately following full doses of sulphapyridine and, although the number was small, experience suggests that further investigation on these lines might be of value.

Treatment by fever induced by mechanical means combined with chemotherapy gives good results in cases of this type, so it is feasible that some cases might be cured by fever of lower level and shorter duration.

The use of T.A.B. vaccine immediately after the first course of chemotherapy appeared at first to be of little value. This method of treatment was regarded as a failure at the time, and was discontinued. However it is interesting to note that the failures responded well to further treatment.

When T.A.B. vaccine was given 3 to 5 weeks after the beginning of treatment the immediate results were better, but the average stay in hospital was longer than in the "failure" group of cases in which T.A.B. vaccine was given immediately following chemotherapy. This point merits further investigation. In most of these cases two divided doses were given with 2 to 4 day intervals.

Non-gonococcal Urethritis.

The same observations apply to these cases as to the

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cases of gonorrhœa, but the results were rather more successful.

Complications of Gonorrhœa and Non-gonococcal Urethritis.

T.A.B. vaccine seemed to give the best results in the cases of arthritis occurring during or following a course of sulphapyridine. In patients with arthritis when admitted to hospital the injections relieved the pain, but in most cases the joints were only temporarily improved. Patients with definite physical signs usually required three treatments with divided doses.

The temperature peak and duration of temperature had some relationship to the clinical result, but the most important point seemed to be the administration of the T.A.B. vaccine at the optimum time in each particular group of cases. The use of fever in conjunction with chemotherapy produced some successes and is worth further investigation. In some groups the optimum time is in doubt and further work must also decide this problem.

SUMMARY AND CONCLUSIONS

The divided dose method of administering T.A.B. vaccine is to be preferred, for the production of higher and longer fever and for the diminution of toxic effects on the patient.

T.A.B. vaccine holds a definite place among methods of treatment of resistant cases of gonorrhœa, non-gonococcal urethritis and their complications. In the treatment of 207 such cases at the Royal Victoria Hospital, Netley, the following conclusions were reached.

1. T.A.B. vaccine alone is useless for cases with persistent gonococcal urethritis, but its use in combination with sulphonamide drugs merits further investigation.

2. T.A.B. vaccine, used late in the treatment of resistant cases of gonorrhœa and urethritis with a persistent urethral discharge and a "dirty" urine, gave good immediate results. Used in similar cases early in treatment, it gave poor immediate results, but many failures in this group were cured by one further course of a sulphonamide drug. The comparative merits of these two methods are still under consideration.

3. T.A.B. vaccine is indicated in resistant cases of arthritis of recent origin and in resistant cases of iritis.

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Arthritic cases are most likely to be cured if this complication has developed during or after chemotherapy, provided that T.A.B. vaccine is given as soon as the signs or symptoms appear, but additional physiotherapy is often necessary.

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TABLE I.—PYREXIAL EFFECT OF SINGLE AND DIVIDED DOSAGE OF T.A.B. VACCINE

No. of Cases	Doses (in Millions)	No. of Treatments with Temperature Peak under 103° F.	No. of Treatments with Temperature Peak over 103° F.	Average No. of Hours over 103° F.	Temperature Peak Average
SINGLE DOSAGE					
10	1st 25 2nd 50	8 2	2 2	1.0	102.2° F.
10	1st 50 2nd 75	7 1	3 —	0.8	102.2° F.
Total of 20 cases		18 (72%)	7 (28%)	0.9	102.2° F.
DIVIDED DOSAGE. (First 50 Cases Treated by this Method.)					
50	1st 25 25 2nd 50 25	4 2	46 36	} 3.8	103.7° F.
Total of 50 cases		6 (7%)	82 (93%)		
SINGLE DOSAGE. (Control Cases.)					
30	1st 250 2nd 500	25 8	5 1	} 0.3	101.9° F.
20	1st 375 2nd 625	17 2	3 2		
Total of 50 cases		52(82.5%)	11(17.5%)	0.4	102.0° F.

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TABLE 1A.—ALL CASES TREATED BY DIVIDED METHOD

No. of Cases Treated	No. of Treatments with Temperature Peak under 103° F.	No. of Treatments with Temperature Peak over 103° F.	Average No. of Hours over 103° F.	Temperature Peak Average
189	75 (23%)	249 (77%)	3.4	103.3° F.

TABLE 2.—PYREXIAL EFFECT OF VARYING VACCINE DOSAGE IN 1ST AND 2ND TREATMENTS IN 180 CASES

No. of Organisms (in millions)	No. of Treatments with Temperature peak under 103° F.	No. of Treatments with Temperature peak over 103° F.
1ST TREATMENT		
10 + 10	5 (71.5%)	2 (28.5%)
25 + 25	38 (29%)	93 (71%)
25 + 50	6 (37.5%)	10 (62.5%)
25 + 25 + 25	4 (26.5%)	11 (73.5%)
2ND TREATMENT		
50 + 25	4 (9%)	40 (91%)
25 + 50	3 (16%)	16 (84%)
25 + 25 + 25	1 (7.5%)	12 (92.5%)
2ND TREATMENT.* (In which 1st Treatment Temperature peak was below 103° F.)		
50 + 25	4 (28.5%)	10 (71.5%)
25 + 25 + 25	1 (9%)	10 (91%)

* Included in above figures.

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TABLE 3.—RESULTS OF T.A.B. VACCINE THERAPY IN CASES OF GONORRHOEA

	No. of Cases	Average No. of Divided Dose Treatments	No. of Cases with at least one Temperature peak over 103° F.	Average No. of days in Hospital
<i>Cases in Group 1.</i>				
Clinical successes . . .	3 (a)	1·7	3	24
Clinical successes with additional local treatment . . .	4 (b)	2·2	3	36
Clinical failures . . .	10	1·8	9	37
<i>Cases in Group 2a.</i>				
Clinical successes . . .	15 (c)	1·5	13	46
Clinical successes with additional local treatment . . .	7	1·5	7	54
Clinical failures . . .	22 (d)	1·8	19	71
<i>Cases in Group 2b.</i>				
Clinical successes . . .	4 (e)	1·8	3	74
Clinical successes with additional local treatment . . .	1	1	0	56
Clinical failures . . .	4	1·8	3	110
<i>Cases in Group 3.</i>				
<i>Given T.A.B. vaccine only.</i>				
Clinical successes . . .	2 (f)	1	1	34
Clinical successes with additional local treatment . . .	—	—	—	—
Clinical failures . . .	16	1·4	15	60
<i>Given T.A.B. combined with Sulphapyridine</i>				
Clinical successes . . .	3 (g)	1	1	75
Clinical successes with additional local treatment . . .	2	2	2	76
Clinical failures . . .	8 (h)	2	7	88

(a) Includes one case of arthritis. (Table 5.)

(b) Includes one case of arthritis. (Table 5.)

(c) Includes two patients with a previous history of arthritis.

(d) Includes eleven patients in whom gonococci appeared in the urethral smear after T.A.B. vaccine, and one patient with stricture of the urethra.

(e) Includes one case of epididymitis.

(f) One patient relapsed, the other received T.A.B. vaccine during a further course of sulphanilamide.

(g) Includes one case of arthritis. (Table 5.)

(h) Includes one patient who later developed epididymitis, but was then cured by T.A.B. vaccine, and one patient who is still in hospital.

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TABLE 4.—RESULTS OF T.A.B. VACCINE THERAPY IN CASES OF NON-GONOCOCCAL URETHRITIS

	No. of Cases	Average No. of Divided Dose Treatments	No. of Cases with at least one Temperature peak over 103° F.	Average No. of days in Hospital
<i>Cases in Group 1.</i>				
Clinical successes . . .	—	—	—	—
Clinical successes with additional local treatment . . .	4 (a)	2.5	4	40
Clinical failures . . .	11	2	11	38
<i>Cases in Group 2a.</i>				
Clinical successes . . .	15	1.5	10	40
Clinical successes with additional local treatment . . .	4	1.5	4	43
Clinical failures . . .	17 (b)	1.8	16	78
<i>Cases in Group 2b.</i>				
Clinical successes . . .	10	1.5	7	58
Clinical successes with additional local treatment . . .	2	1.5	2	48
Clinical failures . . .	2 (c)	2	2	145

(a) Includes one case of arthritis. (Table 5.)

(b) Includes one case of stricture, patient still in hospital.

(c) Includes one case of stricture.

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TABLE 5.—RESULTS OF T.A.B. VACCINE THERAPY IN THE COMPLICATIONS OF GONORRHOEA AND NON-GONOCOCCAL URETHRITIS

	No. of Cases Treated	No. with Symptoms only	Received Physio-therapy	Average No. of Divided Dose Treatments	No. of Cases with at least one Temperature peak over 103° F.	Average No. of days in Hospital
<i>Cases in Group 1a.</i>						
Clinical success .	—	—	—	—	—	—
Improvement .	3	1	2	2·7	3	44
Clinical failure .	7 (a)	1	7	2·3	6	117
<i>Cases in Group 1b.</i>						
Clinical success .	3 (b)	3	3	2·7	2	53
Improvement .	1	1	1	4	1	107
Clinical failure .	—	—	—	—	—	—
<i>Cases in Group 1c.</i>						
Clinical success .	22 (c)	12	3	2	17	43
Improvement .	4	1	4	4·7	4	119
Clinical failure .	—	—	—	—	—	—
<i>Cases in Group 2.</i>						
Improvement .	3 (1 Acute irido-cyclitis). (2 Sub-acute iritis)			4·3	3 (Still at Eye Dept. Out-Patients)	

(a) Includes two patients still in hospital.

(b) Includes one patient in whom urethritis persisted. (Table 4.)

(c) Includes one patient in whom urethritis persisted. (Table 3.)

PYRETO-THERAPY

CHART 1.—SINGLE AND DIVIDED DOSE TREATMENTS
IN SAME PATIENT

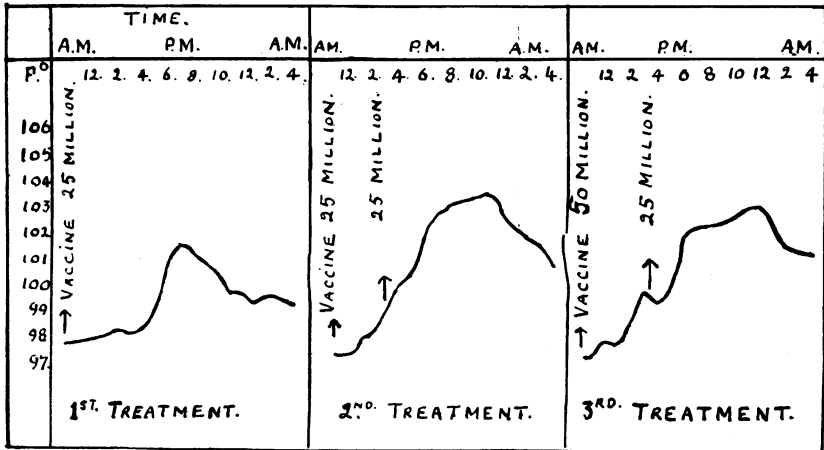
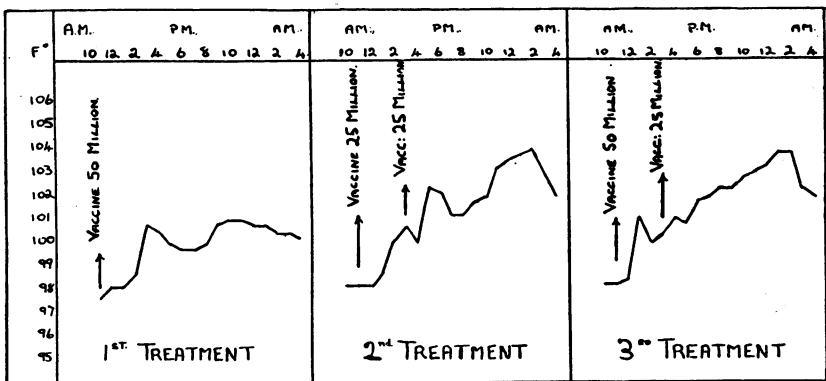


CHART 2.—SINGLE AND DIVIDED DOSE TREATMENTS
IN SAME PATIENT



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CHART 3.—SUCCESSIVE LOW TEMPERATURE PEAKS WITH DIVIDED TREATMENTS IN SAME PATIENT

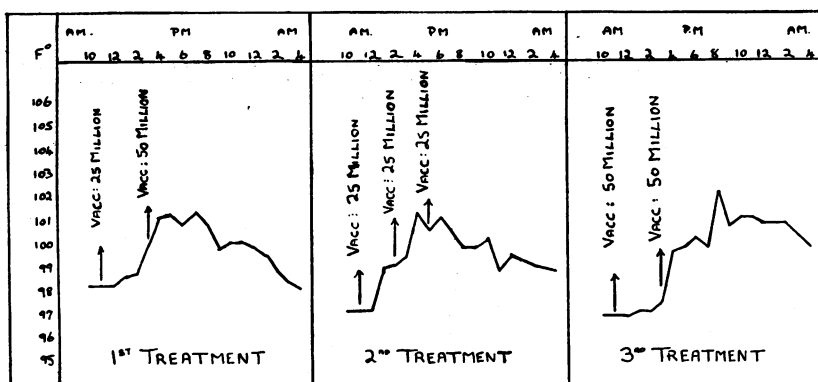


CHART 4.—(a) HIGH TEMPERATURE PEAK AFTER SINGLE DOSE OF T.A.B. VACCINE; (b) HIGH TEMPERATURE PEAK AFTER SINGLE DOSE OF T.A.B. VACCINE IN SECOND TREATMENT

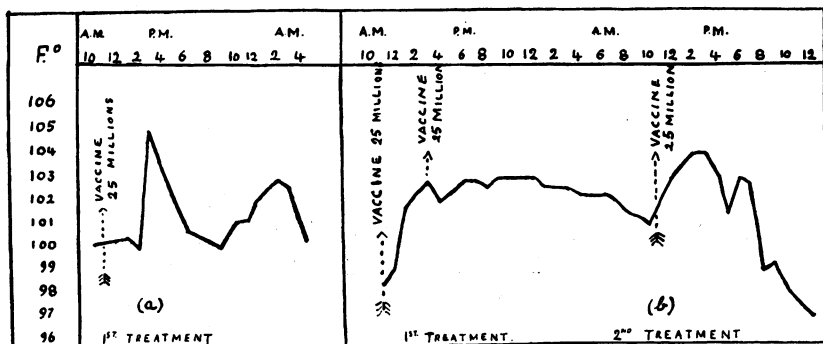


CHART 5.—COMPARISON OF ORAL AND RECTAL TEMPERATURES IN THREE DIFFERENT PATIENTS TREATED BY DIVIDED DOSE METHOD

